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(54) Title: IMMUNOGENIC AND THERAPEUTIC COMPOSITIONS FOR *STREPTOCOCCUS PYOGENES*

(57) Abstract: Group A streptococcal (GAS) antigens useful for providing immunity against *pyogenes* infection.



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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/036009

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07K14/315 A61K39/09 A61K38/7088 A61K39/40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-/--	

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/036009

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 2004/078907 A (INTERCELL AG; MEINKE, ANDREAS; NAGY, ESZTER; WINKLER, BIRGIT; GELBMANN) 16 September 2004 (2004-09-16) page 9, line 49 - page 10, line 21 page 12, line 15 - line 16 page 14, line 3 - line 4 page 22, line 32 - line 39 page 24, line 4 - line 5 page 31, line 31 - page 32, line 22 page 35, line 50 - page 37, line 28 page 39, line 16 - line 30 page 40, line 8 - line 22 spy0019 of SEQ. ID. No. 152 is 100% identical to present GAS5 (SEQ. ID. No. 2). Specific epitopes are disclosed. The encoding DNA of SEQ. ID. No. 2 is 100% identical to present GAS5 (SEQ. ID. No. 651) figure 4a; example 5; tables 1,3</p>	1-40
X	<p>DATABASE UniProt [Online] 1 October 2002 (2002-10-01), XP002367841 retrieved from EBI Database accession no. Q8P318 the whole document</p>	1,24
X	<p>-& NAKAGAWA ICHIRO ET AL: "Genome sequence of an M3 strain of Streptococcus pyogenes reveals a large-scale genomic rearrangement in invasive strains and new insights into phage evolution." GENOME RESEARCH, vol. 13, no. 6a, June 2003 (2003-06), pages 1042-1055, XP002367632 ISSN: 1088-9051 protein SPS0015 SPYM3_0014 is 99,497% identical to present GAS5 over the whole sequence.</p>	1,24
X	<p>DATABASE UniProt [Online] 5 July 2004 (2004-07-05), XP002367842 retrieved from EBI Database accession no. Q7CNQ7 the whole document</p> <p style="text-align: center;">-/--</p>	1,24

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	-& SMOOT J C ET AL: "Genome sequence and comparative microarray analysis of serotype M18 group A Streptococcus strains associated with acute rheumatic fever outbreaks" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 99, no. 7, 2 April 2002 (2002-04-02), pages 4668-4673, XP002267116 ISSN: 0027-8424 SPYM18_0020 is 99,497% identical to present GAS5 over the whole sequence	1,24
P,X	----- DATABASE UniProt [Online] 23 November 2004 (2004-11-23), XP002367843 retrieved from EBI Database accession no. Q5XEL1 the whole document	1,24
X	-& BANKS D J ET AL: "PROGRESS TOWARD CHARACTERIZATION OF THE GROUP A STREPTOCOCCUS METAGENOME: COMPLETE GENOME SEQUENCE OF A MACROLIDE-RESISTANT SEROTYPE M6 STRAIN" JOURNAL OF INFECTIOUS DISEASES, CHICAGO, IL, US, vol. 190, no. 4, 15 August 2004 (2004-08-15), pages 727-738, XP008047099 ISSN: 0022-1899 M6_SPY0017 is 99,497% identical to present GAS5 over the whole sequence	1,24
A	FERRETTI J J ET AL: "Complete genome sequence of an M1 strain of Streptococcus pyogenes" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 98, no. 8, 10 April 2001 (2001-04-10), pages 4658-4663, XP002168716 ISSN: 0027-8424	
A	----- OLIVE C ET AL: "Protection of mice from group A streptococcal infection by intranasal immunisation with a peptide vaccine that contains a conserved M protein B cell epitope and lacks a T cell autoepitope" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 20, no. 21-22, 21 June 2002 (2002-06-21), pages 2816-2825, XP004357806 ISSN: 0264-410X	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/036009

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: —
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 37 and 38 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-40 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Inventions 1-68: claims 1-40 (all partially)

Subject-matter relating to one of the GAS proteins listed in Table 2 in the apparition order in said Table 2, i.e. GAS antigen 5, 6, 18, 22, 23, 25, 29, 30, 36, 49, 56, 60, 62, 63, 65, 67, 68, 69, 74, 75, 76, 77, 78, 81, 82, 85, 86, 89, 91, 92, 93, 94, 96, 97, 98, 99, 100, 101, 103, 104, 105, 108, 123, 131, 142, 143, 158, 165, 166, 175, 178, 179, 187, 188, 190, 195, 205, 206, 207, 218, 219, 242, 249, 271, 291, 327, 380, 685, respectively, as well as to fragments and homologues of said sequences (e.g. GRAB precursor and SPs1285 of Table 11) and to the encoding nucleic acid sequences and antibodies directed to said proteins.

Inventions 69-73: claims 1-40 (all partially)

Subject-matter relating to one of the GAS proteins listed in Table 3 not mentioned in Table 2, in the apparition order in said Table 3, i.e. GAS 73, 74, 109, 129, 130, respectively, as well as to fragments and homologues of said sequence and to the encoding nucleic acid sequences and antibodies directed to said proteins.

Invention 74: claims 1-40 (all partially)

Subject-matter relating to one of the GAS40 protein, in native form or as fusion protein as found in Table 4A-R as well as to fragments and homologues thereof (e.g. as found in Table 5), and to the encoding nucleic acid sequences and antibodies directed to said proteins.

Inventions 75-137: claims 1-40 (all partially)

Subject-matter relating to one of the GAS proteins listed in Table 7 not previously mentioned, in the apparition order in said Table 7, i.e. GAS 4, 15, 16, 24, 54, 57, 64, 72, 84, 102, 152, 157, 163, 168, 177, 191, 192, 193, 194, 198, 201, 224, 251, 259, 262, 264, 268, 277, 282, 299, 382, 405, 406, 425, 433, 460, 469, 493, 500, 545, 558, 587, 645, 650, 362-1, SPY0080a, 0272, 0461, 0611, 0717, 0792, 1029, 1073, 1260, 1613, 1835, 2005, 2093, 2178, GAS45, SPY0047, 0127, 0686, respectively, as well as to fragments and homologues thereof (e.g. M protein type 3 and C5A peptidase precursor of Table 11) and to the encoding nucleic acid sequences and antibodies directed to said proteins.

Inventions 138-160: claims 1-40 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Subject-matter relating to one of the GAS proteins listed in Table 8 not previously mentioned, in the apparition order in said Table 8, i.e. GAS10, 83, 160, 284, 286, 292, 396, SPY0053, 0056, 0063, 0069, 0098, 0666, 0688, 0913, 1200, 1281, 1721, 1750, 1805, 2070, 2092 and g-21909751, respectively, as well as to fragments and homologues thereof and to the encoding nucleic acid sequences and antibodies directed to said proteins.

Inventions 161-162: claims 1-40 (all partially)

Subject-matter relating to one of the GAS proteins listed in Table 9 not mentioned previously, in the apparition order in said Table 9, i.e. NT01SP0246 and GAS309, respectively, as well as to fragments and homologues thereof and to the encoding nucleic acid sequences and antibodies directed to said proteins.

Inventions 163-165: claims 1-40 (all partially)

Subject-matter relating to GAS proteins listed in Table 11 not mentioned previously in apparition order in said Table 11, i.e. SPY1664, GAS149 and SPY0861, respectively, and to fragments and homologues thereof (e.g. putative penicillin binding proteins 2X, putative large conductance mechanosensitive channel and hypothetical protein SPs1270 found in Table 11), and to the encoding nucleic acid sequences and antibodies directed to said proteins.

Inventions 166-180: claims 1-40 (all partially)

Subject-matter relating to the proteins listed in Table 12 considering the references given.

Inventions 181-207: claims 1-40 (all partially)

Subject-matter relating to one of the GAS proteins listed in Table 15 not mentioned previously in the apparition order in said Table 15, i.e. GAS35, 414, 426, 434, 437, 438, 439, 461, 465, 472, 473, 475, 477, 478, 495, 538, 543, 553, 561, 576, 577, 591, 592, 636, 643, 649, 663, respectively, as well as to fragments and homologues thereof, the encoding nucleic acid sequences and antibodies directed to said proteins.

Inventions 208-236: claims 1-40 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Subject-matter relating to the GAS proteins listed in Table 16 not mentioned previously in apparition order of said Table 16, i.e. GAS42, GAS95, M30098, M3_0100, M3_0102, M3_0104, SPs0106, GAS130, GAS137, M6_0157, M6_0159, GAS159, M6_0160, GAS217, 220, 290, 294, 384, 504, 509, 511, 527, 529, 533, 680, 19224134, 19224135, 19224137, 19224141, respectively, as well as to fragments and homologues thereof, the encoding nucleic acid sequences and antibodies directed to said proteins.

Inventions 237-272: claims 1-40 (all partially)

Subject-matter relating to one of the GAS proteins not previously mentioned in the Tables but cited in the claims, in the apparition order in said claims, i.e. NT01SP0102, NT01SP0908 (SPY1111), NT01SP0182 (SPY0216), GAS70, 421, 428, 457, 474, 486, 492, 494, 535, 540, 560, 564, 565, 574, 579, 586, 607, 609, 625, 626, 640, 653, 657, 39, 58, 236, 366, 372, 389, Mprotein, SagA, Sfb1, Shp, respectively, as well as to fragments and homologues thereof, the encoding nucleic acid sequences and antibodies directed to said proteins.

Inventions 273-275: claim 36, partially

Subject-matter relating to the use of an antibody in the manufacture of a medicament for treating *S. pyrogenes* infection, wherein the antibody specifically binds to a surface-exposed GAS antigen which is shorter by at least one amino acid than a GAS protein listed in Table 1 which was not previously mentioned, i.e. GAS41, GAS183 and GAS202, respectively.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2005/036009

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004078907 A	16-09-2004	AU 2004218284 A1 CA 2517518 A1	16-09-2004 16-09-2004